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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,319	04/03/2001	Michael F. Lahn	2879-80	4155

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/17/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/826,319	LAHN ET AL.	
	Examin r	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) 3-8 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,2,9-35 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

1. Claims 1,2,9-35 are under consideration. Claim 1 has been amended.

RESPONSE TO APPLICANTS ARGUMENTS

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1,9-11,18,19,24,25,27,28,31-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Lobb et al. (US Patent 5,871,734) as evidenced by Arrhenius et al. (US Patent 5,869,448) and evidenced by Sato et al.

Lobb et al. teach use of antibody against VLA-4 to treat asthma (see abstract). VLA-4 is a receptor on T cells (see Arrhenius et al., column 63, last paragraph). AHR occurs in asthma (see colum 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Lobb et al. teach use of humanized antiVLA-4 antibody (see column 5, penultimate paragraph). It is an inherent property of said antibody that it does not stimulate T cell activation (said antibodies inhibit VLA-4 function, see column 7, penultimate paragraph). Lobb et al. teach use of monovalent antibody (see column 7, third paragraph). Lobb et al. teach use of antibody dosages encompassed by those recited in claims 18 and 19 (see column 6, penultimate paragraph). Lobb et al. teach administration of said antibody in PBS via nebulized spray (see column 6, penultimate paragraph). Lobb et al. teach the method of claim 27 (see claim 17). Lobb et al. teach the method of claims 28,31,32 (see column 12, Example 2). Lobb et al. teach that the effect seen can be achieved without detectable

blood levels of antibody (see column 12, last paragraph) wherein the antibody would not therefore substantially effect peripheral immune function (eg. because it was not present in the blood). Lobb et al. teach use of said method in humans (see claim 16). Lobb et al. teach that their method resulted in a 70% decrease in inhibition of late phase response which would correlate with the improved FEV1 as per claim 34. Regarding the limitation "inactivation" of T cells, Lobb et al. indicates that anti-VLA-4 antibodies "may attenuate signal transduction necessary for the release of inflammatory mediators and/ or cell chemotactic agents"(see column 6, lines 5-7). Sato et al. confirm that it is an inherent property of certain anti-VLA-4 mabs that they prevent T cell activation (see Figure 1). Sato et al. also indicate that mitogenic VLA-4 antibodies inherently require solid phase crosslinking (see abstract). Lobb et al. teaches use of VLA-4 antibodies which inhibit the VLA-4 mediated signal transduction (see column 7, last paragraph). Thus, it is an inherent property of the antibodies taught by Lobb et al. that they would prevent VLA-4 mediated T cell activation. Thus, the treated T cells would be in a state of inactivation.

Regarding applicants comments about the mode of action of antiVLA-4 antibodies (see page 7 of the instant evidence), there is no evidence of record that supports applicants claim that "It is known in the art that binding of an integrin will not cause depletion or inactivation of T cells.". The MPEP section 2145, section I. (Page 2100-154, Rev. Feb 2003) discloses:

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.").

Furthermore, Lobb et al. indicates that anti-VLA-4 antibodies "may attenuate signal transduction necessary for the release of inflammatory mediators and/ or cell chemotactic agents"(see column 6, lines 5-7). Sato et al. confirm that it is an inherent property of certain anti-VLA-4 mabs that they prevent T cell activation (see Figure 1). Sato et al. also indicate that mitogenic VLA-4 antibodies inherently require solid phase

crosslinking (see abstract). Lobb et al. teaches use of VLA-4 antibodies which inhibit the VLA-4 mediated signal transduction (see column 7, last paragraph). Thus, it is an inherent property of the antibodies taught by Lobb et al. that they would prevent VLA-4 mediated T cell activation. Thus, the treated T cells would be in a state of inactivation.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-3,9-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (US Patent 5,871,734) as evidenced by Arrhenius et al. (US Patent 5,869,448) in view of Schramm et al.

Lobb et al. teach use of antibody against VLA-4 to treat asthma (see abstract). It is a property of VLA-4 that it is a receptor on T cells (see Arrhenius et al., column 63, last paragraph). AHR occurs in asthma (see colum 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Lobb et al. teach use of humanized antiVLA-4 antibody (see column 5, penultimate

paragraph). Said antibody does not stimulate T cell activation (said antibodies inhibit VLA-4 function, see colum 7, penultimate paragraph). Lobb et al. teach use of monovalent antibody (see column 7, third paragraph). Lobb et al. teach use of antibody dosages encompassed by those recited in claims 18 and 19 (see column 6, penultimate paragraph). Lobb et al. teach administration of said antibody in PBS via nebulized spray (see column 6, penultimate paragraph). Lobb et al. teach the method of claim 27 (see claim 17). Lobb et al. teach the method of claims 28,31,32 (see column 12, Example 2). Lobb et al. teach that the effect seen can be achieved without detectable blood levels of antibody (see column 12, last paragraph) wherein the antibody would not therefore substantially effect peripheral immune function (eg. because it was not present in the blood). Lobb et al. teach use of said method in humans (see claim 16). Lobb et al. teach that their method resulted in a 70% decrease in inhibition of late phase response which would correlate with the improved FEV1 as per claim 34. Lobb et al. do not teach use of antiTCR αβ antibodies. Schramm et al. teach use of IV antiTCR αβ antibodies to treat asthma (see abstract). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR αβ) can be used to treat asthma. One of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol. A neutralizing antibody would have been used in the claimed method because Schramm et al. teach that asthma symptoms are reduced in the absence of αβ T cells (see abstract). Regarding the particular dosages of formulation or dosage per weight, a routineer would initially test a wide variety of different dosages in order to have determined the smallest effective dose of the antibody used. A routineer would have administered said antibody

in conjunction with art known treatments for asthma such as those disclosed in column 2, first paragraph of Lobb et al. The antibody would have been administered either before or during asthma symptoms.

Regarding applicants commments, Schramm et al. teach use of IV antiTCR αβ antibodies to treat asthma (see abstract). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR αβ) can be used to treat asthma. One of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol. A neutralizing antibody (eg. an antibody that causes T cell depletion) would have been used in the claimed method because Schramm et al. teach that asthma symptoms are reduced in the absence of αβ T cells (see abstract). Applicants arguments regarding mode of activation antiVLA-4 antibodies have been addressed above. Regarding reasonable expectation of success, Schramm et al. teach use of IV antiTCR αβ antibodies to treat asthma. Lobb et al. teach use of aerosol antibody against VLA-4 to treat asthma. Thus it would be reasonable to assume that since both antibodies have been shown to treat asthma and bind T cells that the antiTCR αβ antibodies could be delivered via aerosol administration. Regarding applicants comments about unexpected results, said comments address functional properties not recited in the claims wherein said arguments are therefore not germane to the claims under consideration. Regarding Fahy et al., Lobb et al. teach use of aerosol antibody against VLA-4 to treat asthma (see abstract and claim 10). Claim 10 is in an issued US Patent and is presumed enabled in the absence of evidence to the contrary. Furthermore, the antibody used in Fahy et al. does not bind a T cell surface antigen and is therefore irrelevant to the claimed invention. It is a property of VLA-4 that it is a receptor on T cells (see Arrhenius et al., column 63, last paragraph). AHR occurs in asthma (see colum 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Regarding the "adaptive immune system", there is no limitation in the claims regarding effects of the instant invention on the "adaptive immune system". Applicant has made a plethora of statements regarding

effects of the claimed invention without providing evidence to support said statements. The MPEP section 2145, section I. (Page 2100-154, Rev. Feb 2003) discloses:

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.").

6. No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644